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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,040

08/29/2006

Friederike Hesse

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HOFFMANN-LA ROCHE INC.  
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EXAMINER

ALLEN, MARIANNE P

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

06/18/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/591,040	<b>Applicant(s)</b> HESSE ET AL.	
	<b>Examiner</b> Marianne P. Allen	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____.                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/29/06</u> .   | 6) <input type="checkbox"/> Other: ____.                          |

## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

The claims are directed to a method for producing NK4 in a microbial host cell by solubilizing inclusion bodies. The methods as written are incomplete. The claims as written recite phosphate buffered solution for solubilizing and renaturing. For example, PBS (phosphate buffered saline) would be encompassed by the claims but would not have been expected to solubilize an inclusion body or renature a denatured protein. The specification describes solubilizing the inclusion bodies by dissolving them over night in a buffer containing 6 M guanidinium hydrochloride, 0.1 M potassium phosphate pH 8.5, 1 mM EDTA, 0.01 mM DTT. The NK4-solubilisate was diluted to a concentration of 0.4 mg / ml in a buffer containing 0.7 M arginine, 0.1 M potassium phosphate pH 8.5, 10 mM GSH, 5 mM GSSG and 1 mM EDTA. The claims do not require any of these denaturing agents. They only require a phosphate buffer. The single example in the specification is insufficient to provide guidance for all phosphate buffered

solutions that would be operable to produce NK4 from inclusion bodies. This example is not commensurate to the scope of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 recite “NK4” without setting forth what this acronym means. It is further unclear if this name corresponds to amino acids 32-494 of SEQ ID NO: 2, amino acids 32 to 478 of SEQ ID NO: 2, sequences that have additional variation within SEQ ID NO: 2, or some other sequence.

Claims 5-6 are confusing in reciting “GSH-modified NK4” as the method steps recited do not require any glutathione (GSH/GSSG).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nesbit (US 2004/0052777) in view of Stahl et al.

Nesbit et al. discloses producing kringle containing fragments of proteins in *E. coli* and purifying them from inclusion bodies using a potassium phosphate buffered solution at pH 7.4 to solubilize and renature. The potassium phosphate buffer is used during the benzamidine sepharose hydrophobic interaction chromatography. The proteins are dialyzed in phosphate buffered saline (PBS) at pH 7.4 for an unspecified amount of time. Nesbit et al. discloses a general method for purifying kringle proteins. (See abstract, claims, and paragraphs [0015-0016, 0125-0126, and 0184-0187]. Nesbit et al. does not disclose producing the N-terminal four kringle containing fragment of HGF (NK4) in *E. coli* and purifying it from inclusion bodies.

Stahl et al. discloses producing the N-terminal four kringle containing fragment of HGF (NK4) in *E. coli* and purifying it from inclusion bodies. Stahl et al. uses a different purification scheme. (See abstract and protein purification section on page 764.)

It would have been obvious to produce NK4 in *E. coli* as disclosed by Stahl et al. and purify it from inclusion bodies as taught by Nesbit et al. One would have been motivated to do so as an alternate method of purification of the protein from a bacterial cell.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1647

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/  
Primary Examiner, Art Unit 1647

mpa